

SECTION X - REGULATORY CONTROL OF RISKS

An analysis of risks associated with total knee arthroplasty reveals that there are some risks inherent to any major surgery, and others that are specific to the device. Generally speaking, complications from infection, pulmonary embolism, gastrointestinal and genitourinary problems are not device specific but are risks associated with most major surgical procedures. For example: A patient infection can be caused by inadequate sterilization of the device but can also be related to a lack of sterile surgical technique. In addition, there are factors, such as pre-existing systemic or localized infection, which can be warned against in the labeling, but may not be alleviated by the physician with pre-operative antibiotics.

This section presents a complete analysis of risks associated with total knee arthroplasty. Risks have been grouped into three general categories: infection, adverse tissue reaction, and loss or reduction of joint function/revision. Patient risks are evaluated in two tables using a common engineering tool, Failure Modes and Effects Analysis (FMEA). Table 5 contains the hazards common to both fixed and mobile bearing knees while Table 6 contains the additional hazards specific to mobile bearing knees, exclusively.

Each FMEA table is organized into three major risk categories; infection, adverse tissue reaction and loss or reduction of joint function/revision. Potential hazards are listed within each category, as applicable. Potential effects from those hazards and an initial risk assessment are presented. Each hazard is then mitigated by one or more solutions or actions designed to reduce the potential risk to the patient. An assessment of the final risk after those solutions/actions are implemented is presented. The goal of FMEA is to reduce each risk to the patient to minimal levels. Finally, special controls are identified for each of the hazards.

Many of the identified risks can be mitigated by material standards, proper device design, labeling and by controlling the device quality through Good Manufacturing Practices (GMP) Quality System Regulations (QSR). Numerous FDA guidance documents, ISO standards, and ASTM standards are available to provide specific guidance regarding materials, testing and labeling.

As documented in Tables 5 and 6, most risks identified are common to fixed bearing and mobile bearing knees. Only two hazards have been identified as unique to mobile bearing knees, and they are related to "loss or reduction of joint function/revision". Specifically, the potential for the mobile bearing to rotate beyond design objectives, and the potential for greater wear due to an additional articulating surface are hazards related to the design of mobile bearing knees.

In addition to the risk analysis, this section also contains information on controls available to mitigate risks:

- **Special Controls to Mobile Bearing Knees:** a review of the requirement for various types of special controls, including a complete listing of FDA guidance documents, ISO Standards, and ASTM Standards that apply to knee prostheses.

- A breakout of guidance documents and standards, assigning each to one of the three general categories of risk (infection, adverse tissue reaction, and loss or reduction of joint function/revision).
- Labeling for mobile bearing knees: a listing of indications, contraindications, warnings, and adverse events relevant to mobile bearing knees, including total knees and unicondylar knees. Also, included is proposed package insert content that includes information on total and unicondylar knees.
- Tests and test methods suggested for mobile bearing knees.

In summary, the sponsor believes that risks associated with mobile bearing knees are known, and can be mitigated to acceptable levels with the general and special controls available to the FDA for other Class II devices.

Risks to Patient Health - FMEA

Table 5: Failure Modes and Effects Analysis for Risks Common to Fixed and Mobile Bearing Knees

1. RISK TO HEALTH: INFECTION

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
		Sev	Prob		Sev	Prob	
Sterility of the implant compromised	Possible patient infection requiring medicinal or surgical intervention (revision)	Maj	M	<ul style="list-style-type: none"> Sterilize implant to a validated sterilization process. Package product in appropriate packaging. Appropriate warnings to conduct an examination of the sterile package prior to use. Physician selection of patients without known local or systemic infection. Strict adherence to sterile surgical technique. Physician administration of perioperative antibiotics. 	Maj	L	<ul style="list-style-type: none"> Updated 510k Sterility Review Guidance K90-1 <u>Ethylene Oxide</u>: ANSI/AAMI/ ISO 11135 -1994 <u>Gamma</u>: ANSI/AAMI/ISO 11137-1994, AAMI TIR27: 2001 and ANSI/AAMI/ ISO TIR15843:2000 Labeling regulations (21 CFR § 801 and § 801 -GMP/QSR), ASTM F-86, F-983 and ISO 6018

2. RISK TO HEALTH: ADVERSE TISSUE REACTION

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
		Sev	Prob		Sev	Prob	
Implant bio-incompatibility or toxicity	Local tissue or systemic reaction requiring medicinal or surgical intervention (revision)	Maj	M	<ul style="list-style-type: none"> Test implant materials and use only if the material passes testing. Use implant materials with long, successful clinical history. 	Maj	L	ISO 10993
Metal sensitivity	Local tissue or systemic reaction requiring surgical intervention (revision)	Mod	M	<ul style="list-style-type: none"> Use implant materials with long, successful clinical history. Conform to materials standards. 	Mod	L	ASTM F-67, F-75, F-136, F-620, F-648, F-799, F-1108, F-1377, F-1472, F-1537, F-1580 and ISO 5832-2/3/4/12
Osteolysis	Implant loosens or bony structure near the implant degrades	Maj	M	<ul style="list-style-type: none"> Use implant materials with long, successful clinical history. Conform to materials standards. Design devices to minimize wear and debris. 	Maj	L	ASTM F-67, F-75, F-136, F-620, F-648, F-799, F-1108, F-1377, F-1472, F-1537, F-1580 and ISO 5832-2/3/4/12, 5834-2
Corrosion of modular metal components	<ul style="list-style-type: none"> Potential revision surgery to remove corroded implants Local tissue reaction due to corrosion debris 	Mod	M	<ul style="list-style-type: none"> Use materials that are compatible for use together. Design implant to minimize motion at any modular metal connections. Conduct corrosion testing to verify design. 	Mod	L	ASTM F-746

3. RISK TO HEALTH: LOSS OR REDUCTION OF JOINT FUNCTION/REVISION

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
		Sev	Prob		Sev	Prob	
Fracture or breakage of knee component	<ul style="list-style-type: none"> Potential revision surgery to remove fractured component Patient pain and/or injury Dislocation 	Maj	M	<ul style="list-style-type: none"> Use implant materials with long, successful clinical history. Conform to materials standards. Design devices to minimize the possibility of fracture. Conduct appropriate testing and/or Finite Element Analysis (FEA). 	Maj	L	<ul style="list-style-type: none"> Guidance documents for “Cemented, semi-constrained total knee prostheses” and “Porous- coated uncemented prostheses.” ASTM F-67, F-75, F-136, F-620, F-648, F-799, F-1108, F-1377, F-1472, F-1537, F-1580 and ISO 5832-2/3/4/12, 5834-2 ASTM F-1800 and ISO 14879-1
Deformation of UHMWPe component	<ul style="list-style-type: none"> Patient pain and/or loss of function Disassociation of UHMWPe component from the tibial baseplate Potential revision surgery to remove deformed components 	Mod	M	<ul style="list-style-type: none"> Conform to materials standards. Conduct contact area and interlock mechanism testing. 	Mod	L	<ul style="list-style-type: none"> Guidance documents for “Cemented, semi-constrained total knee prostheses” and “Porous- coated uncemented prostheses.” ASTM F-648 / ISO 5834-2 (UHMWPe)

3. RISK TO HEALTH: LOSS OR REDUCTION OF JOINT FUNCTION/REVISION (continued)

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
Wear (usually of the UHMWPe articular surface component)	<ul style="list-style-type: none"> Implant loosens or bony structure near the implant degrades Potential revision surgery to remove worn components 	Maj	M	<ul style="list-style-type: none"> Use femoral materials that are designed to articulate with UHMWPe. Conform to materials standards. Process UHMWPe to minimize degradation over time (e.g.: gamma irradiated in inert gas) Process UHMWPe to increase resistance to wear (e.g.: crosslinking). Design components to minimize wear. Conduct wear testing to verify design. 	Maj	L	<ul style="list-style-type: none"> Guidance documents for “Cemented, semi-constrained total knee prostheses” and “Porous- coated uncemented prostheses.” Materials: ASTM F-648 / ISO 5834-2 (UHMWPe) Testing: ASTM F-732, F-1715, F-2025 and ISO 14243-1/2
Delamination of porous coating from metal substrate	<ul style="list-style-type: none"> Prosthesis instability Potential third body wear Potential revision surgery to remove loosened or damaged components 	Maj	M	<ul style="list-style-type: none"> Use implant materials with long, successful clinical history. Conform to materials standards. Design components to minimize the possibility of delamination. Conduct testing to verify design. 	Maj	L	<ul style="list-style-type: none"> “Guidance Document For Testing Orthopedic Implants With Modified Metallic Surfaces Apposing Bone or Bone Cement” Materials: ASTM F-67, F-75, F-136, F-620, F-799, F-1108, F-1377, F-1472, F-1537, F-1580 and ISO 5832-2/3/4/12 ASTM F-1044, F-1147, F-1160, F-1800, F-1854, F-1978 and ISO 14879-1

3. RISK TO HEALTH: LOSS OR REDUCTION OF JOINT FUNCTION/REVISION (continued)

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
Dislocation or disassociation of device or components	<ul style="list-style-type: none"> Patient pain and/or loss of function Potential revision surgery to remove or correct dislocated or failed components 	Maj	M	<ul style="list-style-type: none"> Conduct interlock mechanism and patella testing. Conduct constraint testing. Strict adherence to surgical technique. Design components to minimize potential for dislocation or disassociation (proper size interchangeability) 	Maj	L	<ul style="list-style-type: none"> Guidance documents for “Cemented, semi-constrained total knee prostheses” and “Porous- coated uncemented prostheses.” ASTM F-1223
Delamination of the UHMWPe articular surface component	<ul style="list-style-type: none"> Prosthesis instability Potential revision surgery to remove worn components 	Maj	M	<ul style="list-style-type: none"> Use femoral materials that are designed to articulate with UHMWPe. Conform to materials standards. Process UHMWPe to minimize degradation over time (e.g.: gamma irradiated in inert gas, etc.) Process UHMWPe to increase resistance to delamination (e.g.: crosslinking). Design components to minimize sub-surface stresses that lead to delamination. Conduct delamination testing to verify design. 	Maj	L	ASTM F-648 / ISO 5834-2

3. RISK TO HEALTH: **LOSS OR REDUCTION OF JOINT FUNCTION/REVISION** (continued)

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
		Sev	Prob		Sev	Prob	
Off-Label Use	<ul style="list-style-type: none"> • Device may be damaged and unusable • Potential patient pain or loss of function • Extended surgery time • Prosthesis instability • Potential revision surgery • Device does not function as designed 	Mod	H	<ul style="list-style-type: none"> • Device indications clearly labeled. • Warning in package insert not to use the device off-label. • Instructions for Use (surgical technique) available to physician. • Physician training. 	Mod	M	Labeling regulations (21 CFR § 801 and § 801 -GMP/QSR), ASTM F-86, F-983 and ISO 6018
Incorrect surgical technique	<ul style="list-style-type: none"> • Device is damaged and unusable • Potential patient pain or loss of function • Extended surgery time • Prosthesis instability • Potential revision surgery to remove incorrectly implanted components 	Maj	M	<ul style="list-style-type: none"> • Implants and instrument systems designed to minimize the potential for incorrect implantation. • Instructions for Use (surgical technique) available to physician. • Physician training. • Package insert available to physician. 	Maj	L	Labeling regulations (21 CFR § 801 and § 801 -GMP/QSR), ASTM F-86, F-983 and ISO 6018

3. RISK TO HEALTH: LOSS OR REDUCTION OF JOINT FUNCTION/REVISION (continued)

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
Early component loosening due to inadequate cement layer	<ul style="list-style-type: none"> Prosthesis instability Potential revision surgery to remove loosened components 	Maj	M	<ul style="list-style-type: none"> Rehab protocol specifies proper activities at different periods of time. Appropriate patient or device selection. Appropriate patient or device selection. Instructions for Use (surgical technique) available to physician. Incorporate design features to enhance cement fixation. 	Maj	L	Labeling regulations (21 CFR § 801 and § 801 -GMP/QSR), ASTM F-86, F-983 and ISO 6018
Early component loosening due to incomplete or slow biological ingrowth	<ul style="list-style-type: none"> Prosthesis instability Potential revision surgery to remove loosened components 	Maj	M	<ul style="list-style-type: none"> Rehab protocol specifies proper activities at different periods of time. Appropriate patient or device selection. Confirm good bone quality. Instructions for Use (surgical technique) available to physician. 	Maj	L	Labeling regulations (21 CFR § 801 and § 801 -GMP/QSR), ASTM F-86, F-983 and ISO 6018
Early component failure due to loose joint	<ul style="list-style-type: none"> Prosthesis instability Potential revision surgery to remove failed components or to tighten soft tissues 	Maj	M	<ul style="list-style-type: none"> Appropriate patient or device selection. Follow Instructions for Use (surgical technique). Physician training. 	Maj	L	Labeling regulations (21 CFR § 801 and § 801 -GMP/QSR), ASTM F-86, F-983 and ISO 6018

3. RISK TO HEALTH: **LOSS OR REDUCTION OF JOINT FUNCTION/REVISION** (continued)

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
Incorrect product identification or incorrect sizing	<ul style="list-style-type: none"> Possible confusion concerning the size or type of product Prosthesis instability due to incorrect component matching Increased surgical time 	Mod	M	<ul style="list-style-type: none"> Follow labeling regulations to correctly identify the component. Physician training. Package insert available to physician that shows compatibility of the components. 	Mod	L	Labeling regulations (21 CFR § 801 and § 801 -GMP/QSR), ASTM F-86, F-983 and ISO 6018

Table 6: Failure Modes and Effects Analysis for Mobile Bearing Knees Exclusively

1. RISK TO HEALTH: INFECTION

No risk specific to mobile bearing knees (see Table A - risk is identified along with fixed bearing knees)

2. RISK TO HEALTH: ADVERSE TISSUE REACTION

No risk specific to mobile bearing knees (see Table A – risk is identified along with fixed bearing knees)

3. RISK TO HEALTH: LOSS OR REDUCTION OF JOINT FUNCTION/REVISION

Potential Hazard	Potential Effect	Initial Risk		Solution/Action To Reduce Risk	Final Risk		Pertinent Guidance Document(s) or Standards
		Sev	Prob		Sev	Prob	
Mobile bearing rotates beyond design objectives	<ul style="list-style-type: none"> Prosthesis instability Patient pain or loss of function Potential revision surgery or joint manipulation to remove or realign dislocated components 	Mod	M	<ul style="list-style-type: none"> Design appropriate safeguards (rotational stops, etc.) to prevent “spin-out” of the device or dislocation. Conduct testing to verify design objectives are satisfied. 	Mod	L	None - Industry testing
Greater wear due to additional articulating surfaces	<ul style="list-style-type: none"> Implant loosens or bony structure near the implant degrades Potential revision surgery to remove worn components 	Maj	M	<ul style="list-style-type: none"> Use femoral materials that are designed to articulate with UHMWPe. Conform to materials standards. Process UHMWPe to minimize degradation over time (e.g.: gamma irradiated in inert gas). Process UHMWPe to increase resistance to wear (e.g.: crosslinking). Design components to minimize wear. Conduct wear testing to verify design. 	Maj	L	<ul style="list-style-type: none"> Guidance documents for “Cemented, semi-constrained total knee prostheses” and “Porous-coated uncemented prostheses.” Materials: ASTM F-648 / ISO 5834-2 (UHMWPe) Testing: ASTM F-732, F-1715, F-2025 and ISO 14243-1/2

Special Controls For Mobile Bearing Knees

The sponsors believe that the controls already established for Class II fixed bearing knee devices are sufficient to provide reasonable assurance of safety and efficacy. Class II controls include general controls plus special controls such as performance standards, postmarket surveillance, guidelines, recommendations or other actions deemed necessary by the FDA.

- Performance standards: there are currently no special controls for total knee prostheses. This special control would seem to be unnecessary for mobile bearing knees.
- Postmarket surveillance: the sponsor believes that the existing mandatory medical device reporting (MDR) system is sufficient to provide adequate information to FDA concerning adverse events related to mobile bearing knees. Therefore, postmarket surveillance is unnecessary to reasonably assure the safety and effectiveness of these devices.
- The following is a comprehensive list of special control guidelines and recommended standards to be used, as necessary, by industry when submitting a premarket notification (510[k]).

FDA Guidelines:

1. “Draft Guidance Document for the Preparation of Premarket Notification (510[k]) Applications for Orthopedics Devices – The Basic Elements”;
2. “Guidance for the Preparation of Premarket Notifications (510[k]s) for Cemented, Semi-Constrained Total Knee Prostheses”;
3. “Class II Special Controls Guidance Document: Knee Joint Patellofemorotibial and Femorotibial Metal/Polymer Porous-Coated Uncemented Prostheses; Guidance for Industry and FDA”;
4. “Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement”;
5. “Guidance Document for Testing Non-articulating, ‘Mechanically Locked’ Modular Implant Components”;
6. “Data Requirements for Ultrahigh Molecular Weight Polyethylene (UHMWPe) Used in Orthopedic Devices”;
7. “Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA”;
8. “Data Requirements for Ultrahigh Molecular Weight Polyethylene (UHMWPe) Used in Orthopedic Devices”

International Organization for Standardization (ISO) Consensus Standards:

1. ISO 5832-2, “Implants for Surgery - Metallic Materials - Part 2: Unalloyed Titanium”;
2. ISO 5832-3 “Implants for Surgery – Metallic Materials – Part 3: Wrought Titanium 6-Aluminum 4-Vanadium Alloy”;
3. ISO 5832-4 “Implants for Surgery – Metallic Materials – Part 4: Cobalt-Chromium-Molybdenum Casting Alloy”;

4. ISO 5832-12 “Implants for Surgery – Metallic Materials – Part 12: Wrought Cobalt-Chromium-Molybdenum Alloy”;
5. ISO 5834-2 “Implants for Surgery – Ultra-high Molecular Weight Polyethylene – Part 2: Moulded Forms”;
6. ISO 7207-1, “Implants for Surgery – Femoral and tibial components for partial and total knee-joint prostheses – Part 1: Classification, definitions, and designation of dimensions”;
7. ISO 7207-2, “Implants for Surgery – Components for partial and total knee-joint prostheses – Part 2: Articulating surfaces made of metal, ceramic and plastics materials”;
8. ISO 10993, “Biological Evaluation of Medical Devices Part 1: Evaluation and Testing”;
9. ISO 14243-1, “Implants for Surgery – Wear of total knee-joint prostheses – Part 1: Loading and displacement parameters for wear-testing with load control and corresponding environmental conditions for test”;
10. ISO 14243-2, “Implants for Surgery – Wear of total knee-joint prostheses – Part 2: Methods of measurement”;
11. ISO 14879-1, “Implants for Surgery – Total knee-joint prostheses – Part 1: Determination of endurance properties of knee tibial trays”;
12. ISO 6018 “Orthopedic Implants – General Requirements for Marking, Packaging and Labeling”; and
13. ISO 9001 “Quality Systems – Model for Quality Assurance in Design/Development, Production, Installation and Servicing”

ASTM International Voluntary Consensus Standards:

1. F-67, “Standard Specifications for Unalloyed Titanium for Surgical Implants Applications”;
2. F-75, “Standard Specification for Cast Cobalt-28 Chromium-6 Molybdenum Alloy for Surgical Implant Applications”;
3. F-86, “Standard Practice for Surface Preparation and Marking of Metallic Surgical Implants”;
4. F-136, “Standard Specification for Wrought Titanium-6 Aluminum-4 Vanadium ELI (Extra Low Interstitial) Alloy for Surgical Implant Application”;
5. F-620, “Standard Specification for Alpha Plus Beta Titanium Alloy Forgings for Surgical Implants”;
6. F-648, “Standard Specification for Ultra-High-Molecular-Weight Polyethylene Powder and Fabricated Form for Surgical Implants”;
7. F-732, “Standard Test Method for Wear Testing of Polymeric Materials Used in Total Joint Prostheses”;
8. F-746, “Standard Test Method for Pitting or Crevice Corrosion of Metallic Surgical Implant Materials”;
9. F-799, “Standard Specification for Cobalt – 28 Chromium – 6 Molybdenum Alloy Forgings for Surgical Implants”;
10. F-983, “Standard Practice for Permanent Marking of Orthopedic Implant Components”;
11. F-1044, “Standard Test Method for Shear Testing of Calcium Phosphate Coatings and Metallic Coatings”;
12. F-1108, “Standard Specification for Titanium - 6 Aluminum - 4 Vanadium Alloy Castings for Surgical Implants”;

13. F-1147, “Standard Test Method for Tension Testing of Calcium Phosphate and Metallic Coatings”;
14. F-1160, “Standard Test Method for Shear and Bending Fatigue Testing of Calcium Phosphate and Metallic Medical and Composite Calcium Phosphate/Metallic Coatings”;
15. F-1223, “Standard Test Method for Determination of Total Knee Replacement Constraint”;
16. F-1377, “Standard Specification for Cobalt-28 Chromium-6 Vanadium Powder for Coating of Orthopedic Implants”;
17. F-1472, “Standard Specification for Wrought Titanium – 6 Aluminum – 4 Vanadium Alloy for Surgical Implant Applications”;
18. F-1537, “Standard Specification for Wrought Cobalt – 28 Chromium – 6 Molybdenum Alloys for Surgical Implants”;
19. F-1580, “Standard Specification for Titanium and Titanium-6% Aluminum-4% Vanadium Alloy Powders for Coatings of Surgical Implants”;
20. F-1672, “Standard Specification for Resurfacing Patellar Prosthesis”;
21. F-1715, “Standard Guide for Wear Assessment of Prosthetic Knee Designs in Simulator Devices”;
22. F-1800, “Standard Test Method for Cyclic Fatigue Testing of Metal Tibial Tray Components of Total Knee Joint Replacements”;
23. F-1814, “Standard Guide for Evaluating Modular Hip and Knee Joint Components”;
24. F-1854, “Standard Test Method for Stereological Evaluation of Porous Coatings on Medical Implants”;
25. F-1978, “Standard Test Method for Measuring Abrasion Resistance of Metallic Thermal Spray Coatings by Using the Taber™ Abraser”;
26. F-2025, “Standard Practice for Gravimetric Measurement of Polymeric Components for Wear Assessment”; and
27. F-2083, “Standard Specification for Total Knee Prosthesis”

The FDA guidance and ISO standard documents are appropriate to provide guidance on how to meet general orthopedic device premarket notification (510[k]) and EU medical device requirements, including biocompatibility testing, sterility testing, mechanical performance testing, and physician and patient labeling for mobile bearing knees. Use of the pre-clinical section of the FDA guidance documents can control the risks to health of infection, adverse tissue reaction, loss or reduction of function and/or revision by having manufacturers use surgical quality implant materials, adequately test and sterilize their devices, and provide adequate directions for use and patient information.

Special Controls: Guidance Documents and Standards - Grouped as They Relate to Categories of Risk

1. Infection - Systemic and/or localized infection

Special Controls to Minimize Risk

- “Updated 510(k) Sterility Review Guidance K90-1; Final Guidance for Industry and FDA”
- ANSI/AAMI/ISO 11135-1994 (Ethylene Oxide)
- ANSI/AAMI/ISO 11137-1994, AAMI TIR27:2001 and ANSI/AAMI/ISO TIR15843:2000 (Gamma Radiation)

2. Adverse Tissue Reaction - Implant bio-incompatibility, metal sensitivity, osteolysis and metal corrosion

Special Controls to Minimize Risk

- ASTM material standards: F-67, F-75, F-136, F-620, F-648, F-799, F-1108, F-1377, F-1472, F-1537, F-1580
- ASTM test methods: F-746
- ISO 10993 “Biological Evaluation of Medical Devices – Part I: Evaluation and Testing

3. Loss or Reduction of Joint Function/Revision - Loosening, revision of components, implant failure or fracture, deformation, wear, and dislocation

Special Controls to Minimize Risk

- ASTM material standards: F-67, F-75, F-136, F-620, F-648, F-799, F-1108, F-1377, F-1472, F-1537, F-1580, F-1672, F-2083
- ASTM test methods: F-732, F-746, F-1044, F-1147, F-1160, F-1223, F-1715, F-1800, F-1814, F-1854, F-1978, F-2025
- “Guidance for the Preparation of Premarket Notifications (510[k]s) for Cemented, Semi-Constrained Total Knee Prostheses”
- “Class II Special Controls Guidance Document: Knee Joint Patellofemorotibial and femorotibial Metal/Polymer Porous-Coated Uncemented Prostheses; Guidance for Industry and FDA”
- “Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement”
- 21 CFR § 801 and § 801 - GMP/QSR (Labeling regulations) and ASTM F -86, F-983

Labeling For Mobile Bearing Knees

The following indications for use, contraindications, warnings and adverse effects are consistent with those generally found in current fixed bearing total and unicompartmental knee package inserts.

Mobile Total Knee

Indications for Use:

This device is indicated for:

- Patients with knee pain and disability due to rheumatoid arthritis, osteoarthritis, traumatic arthritis, polyarthritis, collagen disorders and/or avascular necrosis of the femoral condyle
- Post-traumatic loss of joint configuration (particularly when there is patellofemoral erosion, dysfunction, or prior patellectomy)
- Moderate valgus, varus, or flexion deformities
- The salvage of previously failed surgical attempts if the knee can be satisfactorily balanced and stabilized at the time of surgery

The device can be used with or without bone cement.

Contraindications:

Contraindications include:

- Previous history of infection in the affected joint and/or local/systemic infection that may affect the prosthetic joint
- Insufficient bone stock on femoral or tibial surfaces
- Skeletal immaturity
- Neuropathic arthropathy
- Osteoporosis and any loss of musculature or neuromuscular disease that compromises the affected limb
- A stable, painless arthrodesis in a satisfactory functional position
- Severe instability secondary to the absence of collateral ligament integrity

Warnings:

- This device is for single patient use only. Do not reuse.
- Patients should be warned on the impact of excessive loading of the prosthetic knee and the types of activities that are appropriate to minimize the potential for implant failure.
- Do not use this product for other than labeled indications (off-label use).
- Do not use any component if damage is found or caused during setup or insertion.

- Do not use components from other knee systems (and vice versa) unless expressly labeled for such use. Premature wear or loosening may develop and may require surgical explantation.
- The risk of implant failure is higher with inaccurate component alignment or positioning.
- Fat embolism risk is increased with intramedullary instrumentation and/or cement pressurization. Consider venting the femur or tibia.

Potential Adverse Effects:

- Loosening or fracture/damage of the prosthetic knee components or surrounding tissues
- Dislocation and/or joint instability
- Malalignment of the prosthetic knee components
- Bone fracture or nerve damage
- Swelling or infection
- Leg length discrepancies
- Poor range of motion
- Pain
- Venous thromboembolic disease
- Inflammation
- Metal sensitivity
- Corrosion of metal components
- Wear debris can initiate osteolysis which may result in loosening of the implant
- Although there is no conclusive evidence of the relationship between orthopedic implants and malignant tumors, any condition that causes chronic damage to tissues may be oncogenic

Mobile Unicompartmental Knee

Indications for Use:

This device is indicated for:

- Patients with knee pain and disability due to osteoarthritis or traumatic arthritis
- Previous tibial condyle or plateau fractures with loss of anatomy or function
- Varus or valgus deformities
- Use with an intact Anterior Cruciate Ligament (ACL)
- Revision of previous unicompartmental arthroplasty procedures

The device can be used with or without bone cement.

Contraindications:

Contraindications include:

- Previous history of infection in the affected joint and/or local/systemic infection that may affect the prosthetic joint
- Insufficient bone stock on femoral or tibial surfaces
- Skeletal immaturity
- Rheumatoid arthritis
- Neuropathic arthropathy
- Osteoporosis and any loss of musculature or neuromuscular disease that compromises the affected limb
- Varus/valgus deformities greater than 15 degrees
- Chondrocalcinosis
- Damage to the articular cartilage of the opposite compartment

Warnings:

- This device is for single patient use only. Do not reuse.
- Patients should be warned on the impact of excessive loading of the prosthetic knee and the types of activities that are appropriate to minimize the potential for implant failure.
- Do not use this product for other than labeled indications (off-label use).
- Do not use any component if damage is found or caused during setup or insertion.
- Do not use components from other knee systems (and vice versa) unless expressly labeled for such use. Premature wear or loosening may develop and may require surgical explantation.
- The risk of implant failure is higher with inaccurate component alignment or positioning.
- Fat embolism risk is increased with intramedullary instrumentation and/or cement pressurization. Consider venting the femur or tibia.

Potential Adverse Effects:

- Loosening or fracture/damage of the prosthetic knee components or surrounding tissues
- Dislocation and/or joint instability
- Malalignment of the prosthetic knee components
- Bone fracture or nerve damage
- Swelling or infection
- Leg length discrepancies
- Poor range of motion
- Pain
- Venous thromboembolic disease
- Inflammation
- Metal sensitivity
- Corrosion of metal components
- Wear debris can initiate osteolysis which may result in loosening of the implant
- Although there is no conclusive evidence of the relationship between orthopedic implants and malignant tumors, any condition that causes chronic damage to tissues may be oncogenic.

Suggested Package Insert Content for Mobile Bearing Knees

<Device Name> MOBILE BEARING <TOTAL OR UNICOMPARTMENTAL> KNEE

DESCRIPTION

The <device name> consists of <insert a description of the device components and how they inter-relate to each other>.

MATERIALS

Femoral components are made from <insert applicable ASTM metal alloy description>, articular surface components from <insert applicable ASTM plastic description> and tibial baseplates from <insert applicable ASTM metal alloy description>.

INDICATIONS

- This device is indicated for:
 - Patients with knee pain and disability due to rheumatoid arthritis, osteoarthritis, traumatic arthritis, polyarthritis, collagen disorders and/or avascular necrosis of the femoral condyle
 - Post-traumatic loss of joint configuration (particularly when there is patellofemoral erosion, dysfunction, or prior patellectomy)
 - Moderate valgus, varus, or flexion deformities
 - The salvage of previously failed surgical attempts if the knee can be satisfactorily balanced and stabilized at the time of surgery
- The device can be used with or without bone cement.

<When appropriate, substitute the indications for Mobile Unicompartmental Knees>

INDIVIDUALIZATION OF TREATMENT

- Use only instruments and provisionals specifically designed for use with these devices to help ensure accurate surgical implantation, soft tissue balancing, and evaluation of knee function.
- Selection of polyethylene components is a matter of physician discretion. Thicker polyethylene components may be needed if the patient is young, heavy, and/or physically active.

CONTRAINDICATIONS

- Contraindications include:
 - Previous history of infection in the affected joint and/or local/systemic infection that may affect the prosthetic joint
 - Insufficient bone stock on femoral or tibial surfaces
 - Skeletal immaturity
 - Neuropathic arthropathy
 - Osteoporosis and any loss of musculature or neuromuscular disease that compromises the affected limb

- A stable, painless arthrodesis in a satisfactory functional position
- Severe instability secondary to the absence of collateral ligament integrity

<When appropriate, substitute the contraindications for Mobile Unicompartmental Knees>

WARNINGS

- This device is for single patient use only. Do not reuse.
- Do not use:
 - This product for other than labeled indications (off-label use).
 - Any component if damage is found or caused during setup or insertion.
 - Components from other knee systems (and vice versa) unless expressly labeled for such use. Premature wear or loosening may develop and may require surgical explantation.
 - <insert any warnings that are specific to the manufacturer's device>
- The risk of implant failure is higher with inaccurate component alignment or positioning.
- Fat embolism risk is increased with intramedullary instrumentation and/or cement pressurization. Consider venting the femur or tibia.

PRECAUTIONS

- Avoid notching, scratching, or striking the device.
- The potential for deep sepsis can be minimized by using biocontamination controls. Continued surveillance for new or recurrent sources of infection should be continued as long as the device is in place.

ADVERSE EFFECTS

- Loosening or fracture/damage of the prosthetic knee components or surrounding tissues.
- Dislocation and/or joint instability
- Malalignment of the prosthetic knee components
- Bone fracture or nerve damage
- Swelling or infection
- Leg length discrepancies
- Poor range of motion
- Pain
- Venous thromboembolic disease
- Inflammation
- Metal sensitivity
- Corrosion of metal components (the significance and long-term implications are uncertain and await further clinical evidence and evaluation)
- Wear debris can initiate osteolysis which may result in loosening of the implant
- Although there is no conclusive evidence of the relationship between orthopedic implants and malignant tumors, any condition that causes chronic damage to tissues may be oncogenic.

STERILITY

These devices are sterilized by <Indicate type of sterilization>. They remain sterile as long as the package integrity has not been violated. Inspect each package prior to use and do not use the component if any seal or cavity is damaged or breached or if the expiration date has been exceeded. Once opened, the component must be used, discarded, or resterilized.

RESTERILIZATION INFORMATION

- If required, these devices can be resterilized using Association for the Advancement of Medical Instrumentation (AAMI) guidelines and/or Association of Operating Room Nurses (AORN) recommended practices for sterilization. Do not resterilize components that have been contaminated with body fluids or debris or previously implanted.
- <Add any additional resterilization information specific to the device>

PATIENT COUNSELING INFORMATION

Complications and/or failure of mobile knee prostheses are more likely to occur in patients with unrealistic functional expectations, heavy patients, physically active patients, and/or with patients that fail to follow through with the required rehabilitation program. Excessive physical activity and injury can result in loosening, wear, and/or fracture of the knee implant. The patient must be instructed about all postoperative restrictions, particularly those related to occupational and sports activities and about the possibility that the implant or its components may wear out, fail, or need to be replaced. The implant may not, and is not guaranteed to, last the rest of the patient's life. Because prosthetic joints are not as strong, reliable, or durable as natural, healthy joints, all prosthetic knees may need to be replaced at some point.

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician.

Suggested Tests and Test Methods for Mobile Bearing Knees

The following are specific tests that are suggested by the sponsors to establish substantial equivalence in premarket notifications under section 510(k). These tests were derived from the list of guidance documents and standards mentioned previously. Not all tests may be applicable to a given mobile bearing knee design.

1. Biocompatibility

- ISO 10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing"

2. Material Characterization

- UHMWPe components: "Data Requirements for Ultrahigh Molecular Weight Polyethylene (UHMWPe) Used in Orthopedic Devices".

3. Kinematics

- "Guidance for the Preparation of Premarket Notifications (510[k]s) for Cemented, Semi-Constrained Total Knee Prostheses" and "Class II Special Controls Guidance Document: Knee Joint Patellofemoral and femoral tibial Metal/Polymer Porous-Coated Uncemented Prostheses; Guidance for Industry and FDA" which includes the following tests pertaining to kinematics:
 - Data on the expected range of motion for the device;
 - Constraint evaluation (ASTM F-1223 - "Standard Test Method for Determination of Total Knee Replacement Constraint");
 - Contact areas between all interfacing components; and
 - Lateral stability of the patellofemoral joint (a design justification, based upon sound engineering principles, may be substituted for a test report).

4. Fracture, Breakage or Deformation of Components

- ASTM F-1800 ("Standard Test Method for Cyclic Fatigue Testing of Metal Tibial Tray Components of Total Knee Joint Replacements").
- "Draft Guidance for the Preparation of Premarket Notifications for Cemented, Semi-constrained Total Knee Prostheses" and "Class II Special Controls Guidance Document: Knee Joint Patellofemoral and femoral tibial Metal/Polymer Porous-Coated Uncemented Prostheses; Guidance for Industry and FDA" which includes the following tests pertaining to fracture, breakage or deformation. A design justification, based upon sound engineering principles, may be substituted for test reports.

- Ability of any interlock mechanism to survive physiological loads;
- Fatigue strength of the tibial component under worst case physiological loading conditions;
- Shear fatigue strength of metal-backed patella components (if applicable);
- Static tensile strength of metal-backed patella components (if applicable);
- Shear fatigue testing of the UHMWPe posterior stabilized tibial baseplate post (if applicable);

5. Corrosion of Metal Components

- ASTM F-746, ("Standard Test Method for Pitting or Crevice Corrosion of Metallic Surgical Implant Materials")

6. Cyclic Wear

- “Guidance for the Preparation of Premarket Notifications (510[k]s) for Cemented, Semi-Constrained Total Knee Prostheses” and “Class II Special Controls Guidance Document: Knee Joint Patellofemorotibial and femorotibial Metal/Polymer Porous-Coated Uncemented Prostheses; Guidance for Industry and FDA” which includes the following tests pertaining to wear.
 - Wear - If the polyethylene tibial insert has a minimum thickness under the condyles of less than 6 mm, then wear testing must be conducted demonstrating the ability of the insert to survive 5 million cycles (modified by the FDA from the original 10 million cycles) of physiological loading in a knee simulator. The simulator should provide sliding, rolling and rotational movements.
 - Use as wear test guides: ASTM F-1715, ("Standard Guide for Wear Assessment of Prosthetic Knee Designs in Simulator Devices") or ISO 14243-1, ("Implants for surgery – Wear of total knee-joint prostheses – Part 1: Loading and displacement parameters for wear-testing with load control and corresponding environmental conditions for test").
 - Use as wear assessment guides: ASTM F-2025, ("Standard Practice for Gravimetric Measurement of Polymeric Components for Wear Assessment") or ISO 14243-2, ("Implants for surgery – Wear of total knee-joint prostheses – Part 2: Methods of measurement")

7. Porous Coating

- “Guidance document for Testing Orthopedic Implants with Modified Metallic Surfaces Apposing Bone or Bone Cement” which includes the following tests pertaining to the porous coating:
 - Shear fatigue of the porous coating to 10 million cycles;
 - ASTM F-1044 (“Standard Test Method for Shear Testing of Calcium Phosphate Coatings and Metallic Coatings”);
 - ASTM F-1147 (“Standard Test Method for Tension Testing of Calcium Phosphate and Metallic Coatings”);
 - ASTM F-1160 (“Standard Test Method for Shear and Bending Fatigue Testing of Calcium Phosphate and Metallic Medical and Composite Calcium Phosphate/Metallic Coatings”);
 - ASTM F-1978, “Standard Test Method for Measuring Abrasion Resistance of Metallic Thermal Spray Coatings by Using the TaberTM Abraser”;
 - Plastic deformation of the porous coating.

8. Other Tests

- The FDA may require other tests to establish substantial equivalence on a case-by-case basis.